Claims

1. A combined preparation for simultaneous, separate or sequential use as a contrast agent in ultrasound imaging, said preparation comprising:

i) a first composition which is an injectable aqueous medium comprising dispersed gas and material serving to stabilise said gas; and

ii) a second composition which is an injectable oil-in-water emulsion wherein the oil phase comprises a diffusible component capable of diffusion *in vivo* into said dispersed gas so as at least transiently to increase the size thereof, said composition further comprising material serving to stabilise said emulsion,

characterised in that material present at the surfaces of the dispersed gas phase and material present at the surfaces of the dispersed oil phase have opposite charges and thereby have affinity for each other.

2. A combined preparation as claimed in claim 1 wherein the dispersed gas comprises air, nitrogen, oxygen, carbon dioxide, hydrogen, an inert gas, a sulphur fluoride, selenium hexafluoride, an optionally halogenated silane, an optionally halogenated low molecular weight hydrocarbon, a ketone, an ester or a mixture of any of the foregoing.

3. A combined preparation as claimed in claim 2 wherein the gas comprises sulphur hexafluoride or a perfluorocarbon.

4. A combined preparation as claimed in claim 3 wherein said perfluorocarbon is perfluoropropane, perfluorobutane or perfluoropentane.

5. A combined preparation as claimed in claim 1 wherein the dispersed gas is stabilised by a

coalescence-resistant surface membrane, a filmogenic protein, a polymer material, a non-polymeric and non-polymerisable wall-forming material or a surfactant.

6. A combined preparation as claimed in claim 5 wherein said surfactant comprises at least one phospholipid.

7. A combined preparation as claimed in claim 6 wherein at least 75% of said surfactant comprises phospholipid molecules individually bearing net overall charge.

8. A combined preparation as claimed in claim 7 wherein at least 75% of the surfactant comprises one or more phospholipids selected from phosphatidylserines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids and cardiolipins.

9. A combined preparation as claimed in claim 8 wherein at least 80% of said phospholipids comprise phosphatidylserines.

10. A combined preparation as claimed in claim 1 wherein the diffusible component comprises an aliphatic ether, polycyclic oil, polycyclic alcohol, heterocyclic compound, aliphatic hydrocarbon, cycloaliphatic hydrocarbon or halogenated low molecular weight hydrocarbon, or a mixture of any of the foregoing.

11. A combined preparation as claimed in claim 10 wherein the diffusible component comprises one or more perfluorocarbons.

12. A combined preparation as claimed in claim 11 wherein said perfluorocarbon(s) comprise one or more perfluoroalkanes, perfluoroalkenes,

perfluorocycloalkanes, perfluorocycloalkenes and/or perfluorinated alcohols.

13. A combined preparation as claimed in claim 12 wherein the diffusible component comprises one or more perfluoropentanes, perfluorohexanes, perfluorodimethylcyclobutanes and/or perfluoromethylcyclopentanes.

14. A combined preparation as claimed in claim 1 wherein the diffusible component emulsion is stabilised by a phospholipid or lipopeptide surfactant.

15. A combined preparation as claimed in claim 1 wherein the first composition contains anionic surface material and the second composition contains cationic surface material.

16. A combined preparation as claimed in claim 15 wherein said anionic material is a negatively charged phospholipid and said cationic material is a lipophilic quaternary ammonium salt, a lipophilic pyridinium salt, a lipophilic primary, secondary or tertiary amine, a fatty acid amide of an optionally substituted di- or tri-amine, a fatty alcohol ester of an amino acid or a positively charged phospholipid or lipopeptide.

17. A combined preparation as claimed in claim 16 wherein said cationic material is present as an additive to the stabilising material of the second composition.

18. A combined preparation as claimed in claim 1 which further includes a vasodilator and/or vasoconstrictor drug.

19. A combined preparation as claimed in claim 18 wherein said vasodilator drug is adenosine.

20. A combined preparation as claimed in claim 1 which further includes a therapeutic agent.

21. A combined preparation as claimed in claim 1 which further includes contrast-enhancing moieties for an imaging modality other than ultrasound.

22. A method of generating enhanced images of a human or non-human animal subject which comprises the steps of:

i) injecting a first composition as defined in claim 1 into the vascular system of said subject;

ii) before, during or after injection of said first composition injecting a second composition as defined in claim 1 into said subject; and

iii) generating an ultrasound image of at least a part of said subject.

23. A method as claimed in claim 22 wherein microbubble growth from the contrast agent is activated within the subject by application of external activation.

24. A method as claimed in claim 23 wherein said external activation comprises ultrasound irradiation.

25. A method as claimed in claim 22 wherein a vasodilator or vasoconstrictor drug is coadministered to the subject.

26. A method as claimed in claim 25 wherein said vasodilator drug is adenosine.